Multiple targets of miR-302 and miR-372 promote reprogramming of human fibroblasts to induced pluripotent stem cells.

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Public Summary:

Scientific Abstract:
The embryonic stem cell-specific cell cycle-regulating (ESCC) family of microRNAs (miRNAs) enhances reprogramming of mouse embryonic fibroblasts to induced pluripotent stem cells. Here we show that the human ESCC miRNA orthologs hsa-miR-302b and hsa-miR-372 promote human somatic cell reprogramming. Furthermore, these miRNAs repress multiple target genes, with downregulation of individual targets only partially recapitulating the total miRNA effects. These targets regulate various cellular processes, including cell cycle, epithelial-mesenchymal transition (EMT), epigenetic regulation and vesicular transport. ESCC miRNAs have a known role in regulating the unique embryonic stem cell cycle. We show that they also increase the kinetics of mesenchymal-epithelial transition during reprogramming and block TGFbeta-induced EMT of human epithelial cells. These results demonstrate that the ESCC miRNAs promote dedifferentiation by acting on multiple downstream pathways. We propose that individual miRNAs generally act through numerous pathways that synergize to regulate and enforce cell fate decisions.